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Electrical impedance spectroscopy with optimised electrode configurations for 3D tissue engineering applications

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The current advances in biotechnological research have led to an increasing demand for solid analytical methods focusing on applications within the fields of tissue engineering, biomaterial science and 3D cell cultures. Furthermore, in vitro studies on cell functionality require a physiologically representative microenvironment in terms of extracellular matrix and controlled biochemical and biomechanical parameters. A major challenge in this regard is the monitoring of cellular proliferation within 3D scaffolds, which provide a platform for cell growth and cell-cell interaction in all three dimensions. Although traditional optical microscopic techniques are unsuitable for monitoring thick 3D constructs, electrical impedance spectroscopy (EIS) has been proven to be a sensitive, label-free and minimally invasive method for characterising passive electrical properties of biomaterials and biological systems both in vivo and in vitro.

We developed different EIS-based methods for real-time monitoring of 3D cell cultures embedding vertical plate and needle electrodes for static and perfusion-based cell culturing. Electrodes can be used in a multiplexing-like approach with different 2, 3 and 4 terminal configurations[1] to gain information about their spatial distribution in a 3D environment. The same setup can be used for characterising the scaffold architecture[2] and also estimating the influence of mammalian cell proliferation on medium conductivity. Optimised protocols for electrode functionalisation were developed using aqueous solvents to eliminate protein and cell adhesion to enhance detection reproducibility and electrode reusability. Validation with finite element simulations, phantom experiments mimicking cell clusters and cell-based experiments were performed aiming to incorporate spatial-enhanced 3D sensing into miniaturised perfusion bioreactors for real-time monitoring of cell proliferation in porous scaffolds.

References

1. Canali C. et al. 2015. Biosens. Bioelectron. 63, 72–79
2. Canali C. et al. 2015 Electroanalysis. 27, 193–199